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10/551,052	07/13/2006	Katsumi Mochitate	053111	1427

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WESTERMAN, HATTORI, DANIELS & ADRIAN, LLP
1250 CONNECTICUT AVENUE, NW
SUITE 700
WASHINGTON, DC 20036

EXAMINER	
HANLEY, SUSAN MARIE	

ART UNIT	PAPER NUMBER
1653	

NOTIFICATION DATE	DELIVERY MODE
10/07/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentmail@whda.com

Office Action Summary	Application No.	Applicant(s)	
	10/551,052	MOCHITATE, KATSUMI	
	Examiner	Art Unit	
	SUSAN HANLEY	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1 and 17-34* is/are pending in the application.

5a) Of the above claim(s) *26-34* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1 and 17-25* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1 and 17-34 are pending.

Election/Restrictions

Upon further consideration, the restriction between groups I and II, mailed 4/15/2009, is withdrawn. Claims 26-34 stand withdrawn.

Claims 1 and 17-25 are under examination.

Withdrawal of Rejections

The response and amendment filed 5/16/2011 are acknowledged. The rejections not explicitly restated below are withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 is rejected because the phrase "the solidified preparation" lacks antecedent basis in claim 1.

Claims 18-25 are rejected because they are dependent claims that do not overcome the deficiencies of the rejected claim from which they depend.

Claim Rejections - 35 USC § 103

Claims 1 and 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Matsuura et al. (US 2004/0082001) in view of evidence from Kleinsek et al. (US 20070065415) in view of Frutos et al. (US 2004/0043508; previously cited) and Rodriguez et al. (US 20010007001).

Matsuura et al. teach an assay for anti-laminin antibody wherein a sample is allowed to react with laminin-1 or a fragment thereof (section [0011]). The laminin-1 (instant claim 19) for the assay is immobilized on a carrier which can be a synthetic organic polymer including styrene-maleic anhydride copolymer (MAST) from a genus of 12 polymers (section 0025]). Kleinsek et al. teach that laminin-1 comprises the RGD motif for cell attachment (section [0138]).

Matsurra et al. do not teach that the laminin-1 is immobilized on a styrene-maleic anhydride copolymer that is coated on a substrate (claim 1) wherein the immobilization between the laminin-1 and the polymer is covalent between a functional group that can reacte with a protein or peptide (claim 17) such as amide bonding (claim 18).

Frutos et al. teach a substrate which has a reactive surface to which a polymer coating is covalently bound (section [0006]). Various types of biomolecules can be immobilized on the polymer including proteins from a genus of eight, including cells and proteins (section [0010]). The biomolecule is attached to the polymer coating by covalent binding (claim 17), electrostatic binding or a combination thereof (section 0010]). Frutos et al. disclose a glass slide having a coating of poly[styrene-co-maleic anhydride] (MAST) disposed thereon (last two lines of section [0042]). Oligonucleotides

wherein immobilized on the MAST polymer (section ([0042]). Frutos et al. do not specifically teach that the reaction is though the anhydride functionality of the MAST polymer but disclose that “Residual anhydride groups were blocked …” (section [0046]). From this disclosure the ordinary artisan would reasonably conclude that the maleic anhydride reacted with the oligonucleotides to form a covalent bond which resulted in the immobilization of the oligonucleotides.

Rodriguez et al. teach that maleic anhydride forms amide bonds (section [0052]; instant claim 18).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the MAST-coated substrate taught by Frutos et al. as the carrier to which laminin-1 is immobilized by amide bonding for the assay taught by Matsurra et al., thus meeting the limitations of instant claims 1, 17 and 18. The ordinary artisan would have been motivated to do so because each carrier is known to have the same function, binding of biomolecules including proteins. Hence, the substitution is no more than the predictable use of prior art elements according to their established functions resulting in the simple substitution of one known element for another for a predictable result. The ordinary artisan would have had a reasonable expectation that one could successfully employ the MAST-substrate taught by Frutos et al. as the carrier for laminin-1 since Frutos et al. teach that the carrier is suitable for the immobilization of proteins.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to form amide bonds between the amino groups of the laminin-1 and the carbonyl groups of the maleic anhydride to immobilize the laminin-1 to the MAST substrate taught by Frutos. The ordinary artisan would have been motivated to do so because Frutos et al. specifically recommend using covalent bonding of the polymer (e.g., MAST) to a biomolecule for immobilization. The ordinary artisan would have had a reasonable expectation that one could form an amide bond between the amino groups of a protein and maleic anhydride because Rodriguez et al. report that maleic anhydride forms amide bonds.

The references are silent regarding the hydrophobic-absorptive and cell binding characteristics of laminin-1 to cells but meets the claimed limitations in that MAST is a linear polymer with a hydrophobic styrene group and that laminin-1 is bound to a MAST substrate which indicates that the claimed characteristics should be present in the prior art invention as also as those instantly claimed.

Furthermore Kleisnsek et al. teach that laminin-1 comprising RGD which attaches cells which indicates that the claimed characteristics should be present in the prior art invention as also as those instantly claimed. In this case, burden is shifted to the Applicant to distinguish the instant invention over the prior art.

It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe naturally includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants

to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

It is noted that claim 1 has the intended use of a substrate for culturing adherent cells. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In the instant case, laminin-1 comprises RGD which attach cells to a substrate.

Regarding the publication date of Kleinsek et al., the critical date of extrinsic evidence showing a universal fact need not antedate the filing date. As discussed in MPEP § 2124:

> In certain circumstances, references cited to show a universal fact need not be available as prior art before applicant's filing date. In re Wilson, 311 F.2d 266, 135 USPQ 442 (CCPA 1962). Such facts include the characteristics and properties of a material or a scientific truism. Some specific examples in which later publications showing factual evidence can be cited include situations where the facts shown in the reference are evidence "that, as of an application 's filing date, undue experimentation would have been required, In re Corneil, 347 F.2d 563, 568, 145 USPQ 702, 705 (CCPA 1965), or that a parameter absent from the claims was or was not critical, In re Rainer, 305 F.2d 505, 507 n.3, 134 USPQ 343, 345 n.3 (CCPA 1962), or that a statement in the specification was inaccurate, In re Marzocchi, 439 F.2d 220, 223 n.4, 169 USPQ 367, 370 n.4 (CCPA 1971), or that the invention was inoperative or lacked utility, In re Langer, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA 1974), or that a claim was indefinite, In re Glass, 492 F.2d 1228,1232 n.6, 181 USPQ 31, 34 n.6 (CCPA 1974), or that characteristics of prior art products were known, In re Wilson, 311 F.2d 266, 135 USPQ 442 (CCPA 1962)." In re Koller, 613 F.2d 819, 823 n.5, 204 USPQ 702, 706 n.5 (CCPA 1980) (quoting In re Hogan, 559 F.2d 595, 605 n.17, 194 USPQ 527, 537 n.17 (CCPA 1977) (emphasis in original)). However, it is impermissible to use a later factual reference to determine whether the application is enabled or described as required under 35 U.S.C. 112, first paragraph. In re Koller, 613 F.2d 819, 823 n. 5, 204 USPQ 702, 706 n.5 (CCPA 1980). References which do not qualify as prior art because they postdate the

> claimed invention may be relied upon to show the level of ordinary skill in the art at or around the time the invention was made. Ex parte Erlich, 22 USPQ 1463 (Bd. Pat. App. & Inter. 1992).

In the instant case, Kleinsek et al. disclose teach that laminin-1 naturally comprises the RGD sequence.

Claims 1, 17-21 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Borenstein et al. (US 20020182241) in view of Frutos et al. (US 2004/0043508; previously cited) and Rodriguez et al. (US 20010007001).

Borenstein et al. teach that cell adhesion to a surface can be mediated by specie cell surface adhesion molecules. Cells that attach to fibronectin can be made to attach by coating the regions of initial cell adhesion with fibronectin (instant claim 19) or RGD (instant claim 20) which binds to a fibronectin receptor or by an engineered protein (the peptide comprises RGD which has three amino acids (instant claim 25). The limitations of instant claim 21 are met since the peptide RGD has the specific sequence RGD. Hence, it is related to fibronectin which binds to an integrin receptor on a cell side. Regions for cell adhesion can also be coated with laminin, fibronectin, collagen, vitronectin, or others (instant claim 19; section [0149]).

Borenstein et al. do not teach that the cell adhesive protein (laminin, fibronectin, vitronectin, or collagen) or peptide (RGD) is immobilized on a styrene-maleic anhydride copolymer that is coated on a substrate (claim 1) for the site of cell immobilization wherein the binding is covalent between a functional group that can reacted with a protein or peptide (claim 17) such as amide bonding (claim 18).

The disclosures by Frutos et al. and Rodriguez et al. are discussed supra. It is again noted that Frutos et al. teach that the disclosed substrate is for attaching proteins or cells.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the MAST-coated substrate taught by Frutos et al. as the site of cell immobilization to which the disclosed cell binding proteins or RGD are immobilized by amide bonding, thus meeting the limitations of instant claims 1, 17 and 18. The ordinary artisan would have been motivated to do so because Frutos et al. specifically teach that the polymer substrates, including MAST, are suitable for protein and cell immobilization. The ordinary artisan would have been motivated to select MAST as the polymer coated on the substrate since it can form amide bonds with the amino groups of proteins. The ordinary artisan would have had a reasonable expectation that one could successfully employ the MAST-substrate taught by Frutos et al. as the site of initial cell adhesion in the method of Boresnstein et al. since Frutos et al. teach that the carrier is suitable for the immobilization of proteins as well as cells.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to form amide bonds between the amino groups of the disclosed RGD peptide or proteins that adhere cells taught by Borenstein et al. and the carbonyl groups of the maleic anhydride to immobilize the said proteins or RGD peptide to the MAST- substrate taught by Frutos. The ordinary artisan would have been motivated to do so because Frutos et al. specifically recommends using covalent bonding of the polymer (e.g., MAST) that covers the substrate to a biomolecule for immobilization. The

ordinary artisan would have had a reasonable expectation that one could form an amide bond between the amino groups of a protein or peptide and maleic anhydride because Rodriguez et al. teach that maleic anhydride forms amide bonds.

The references are silent regarding the hydrophobic-absorptive and cell binding characteristics of laminin-1 to cells but meets the claimed limitations in that MAST is a linear polymer with a hydrophobic styrene group and that laminin-1 is bound to a MAST substrate which indicates that the claimed characteristics should be present in the prior art invention as also as those instantly claimed. In this case, burden is shifted to the Applicant to distinguish the instant invention over the prior art.

It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe naturally includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Claims 1 and 17-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nomizu et al. (1996), Okazaki et al. (2002; Peptide Sci. 38: 213-216), Makino et al. (1999), Kadoya et al. (2003), Okazaki et al. (2002; J. Biol. Chem. 277: 37070-37078; referred to as Okazaki2), Atani et al. (2001) or Kato et al. (2001) in view of Frutos et al. (US 2004/0043508; previously cited) and Rodriguez et al. (US 20010007001).

Nomizu et al. teach synthetic peptides derived from the alpha G domain of laminin (abstract; instant claim 23) that are coated on round bottom glass plates or sepharose beads) for the attachment of cells (p. 38-39). It is disclosed that peptides AG-73 (SEQ ID No. 1; instant claim 24), MG-73 (SEQ ID No. 5; instant claim 24), FIB-1 (SEQ ID No. 16; instant claim 22; and Laminin-1 (instant claim 19) attached cells (Table 1 and Fig 2). The synthetic peptides are 112mers, meeting the limitation of instant claim 25. They are cell adhesion binding regions related to laminin (instant claim 20). The limitations of instant claim 21 are met since the peptide FIB-1 has the specific sequence RGD. Hence, it is related to fibronectin which binds to an integrin receptor on a cell side.

Okazaki et al. teach synthetic peptides derived from the alpha 4 G domain of laminin (abstract; instant claim 23) that are coated on round bottom glass plates or sepharose beads) for the attachment of cells (p. 216). It is disclosed that peptides AG-73 (SEQ ID No. 1; instant claim 24), A4G78 (SEQ ID No. 20; instant claim 24), A4G82 (SEQ ID No. 7) attached cells (Table 1). The synthetic peptides are 12mers, meeting the limitations of instant claim 25. They are cell adhesion binding regions related to laminin (instant claim 20).

Makino et al. teach synthetic peptides derived from the alpha 5 G domain of laminin (instant claim 23) that are coated on plastic plates for the attachment of cells (abstract). It is disclosed that peptides A5G-71 (SEQ ID No. 9; instant claim 24), A5G73 (SEQ ID No. 10; instant claim 24), A5G77 (SEQ ID No. 12) attached cells (fig. 1). The synthetic peptides are 12mers, meeting the limitations of instant claim 25. They are cell adhesion binding regions related to laminin (instant claim 20).

Kadoya et al. teach the testing of peptides derived by laminin-alpha5 chain LG4 module (reasonably interpreted to be the G-domain (p. 154, bottom of the left column). The peptides were coated onto a 96-well plates. HT 1080 cells were plated onto the peptide-coated wells under serum-free conditions and attachment was determined (p. 155, bottom of left column). It is disclosed that the peptides that were immobilized were A5G77 (SEQ ID No. 12), A3G75 (SEQ ID No. 21) and A5G77f (SEQ ID No. 18). The synthetic peptides are 12mers, meeting the limitations of instant claim 25. They are cell adhesion binding regions related to laminin (instant claim 20).

Okazaki2 teach synthetic peptide AG73 (fig. 2; SEQ ID No. 19; instant claim 24) derived from the alpha 4 G domain of laminin that is coated on sepharose beads for the attachment of cells (p. 37073; left col. 5th full paragraph). The synthetic peptide is a 12mer, meeting the limitations of instant claim 25. It is a region related to laminin (instant claim 20).

Atani et al. teach synthetic peptide A3G83 (fig. 2; SEQ ID No. 15; instant claim 24) derived from the alpha 3 G domain of laminin (title of the reference) that is coated on a 96-well plate for the attachment of cells (p. 28781-28782, joining paragraph). The synthetic peptide is a 12mer, meeting the limitations of instant claim 25. It is a region related to laminin (instant claim 20).

Kato et al. teach synthetic peptide AG73T (Table 1; SEQ ID No. 2; instant claim 24) derived from the alpha G domain of laminin (title of the reference) that is coated on a plate for the attachment of cells (p. bottom of p. 252). The synthetic peptide is a

12mer, meeting the limitations of instant claim 25. It is a region related to laminin (instant claim 20).

Neither Nomizu et al., Okazaki et al., Okazaki2, Makino et al., Kadoya et al., Atani et al. nor kato et al. teach that laminin-1 or the synthetic peptides are immobilized on a styrene-maleic anhydride copolymer that is coated on a substrate (claim 1) wherein the binding is covalent between a functional group that can reacted with a protein or peptide (claim 17) such as amide bonding (claim 18).

The disclosures by Frutos et al. and Rodrigues et al. are discussed supra. It is again noted that Frutos et al. teach that the disclosed polymer substrates are suitable for cell attachment.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the MAST-coated substrate taught by Frutos et al. as the carrier to which laminin-1 or the synthetic peptides taught by Nomizu et al., Okazaki et al., Okazaki2, Makino et al. Kadoya et al., Atani et al. or Kato et al. are immobilized by amide bonding for the for the cell attachment studies of Nomizu et al., Okazaki et al., Okazaki2, Makino et al. Kadoya et al., Atani et al. or Kato et al., thus meeting the limitations of instant claims 1, 17 and 18. The ordinary artisan would have been motivated to do so because each carrier (the substrate of Frutos et al. and the 96-well plates, glass plates, plastic plates or beads taught by Nomizu et al., Okazaki et al., Okazaki2, Makino et al. Kadoya et al., Atani et al. or Kato et al. are known to have the same function, serving as a substrate on which a cell binding protein or peptide is immobilized to attach cells thereto. Hence, the substitution is no more than the

predictable use of prior art elements according to their established functions resulting in the simple substitution of one known element for another for a predictable result. The ordinary artisan would have had a reasonable expectation that one could successfully employ the MAST-substrate taught by Frutos et al. as the carrier for laminin-1 or the synthetic peptides taught by Nomizu et al., Okazaki et al., Okazaki2, Makino et al. Kadoya et al., Atani et al. or Kato et al. since Frutos et al. teach that the carrier is suitable for the immobilization of proteins and cells.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to form amide bonds between the amino groups of laminin-1 or the synthetic peptides taught by Nomizu et al., Okazaki et al., Okazaki2, Makino et al. Kadoya et al., Atani et al. or Kato et al. and the carbonyl groups of the maleic anhydride to immobilize the laminin-1 to the MAST substrate taught by Frutos. The ordinary artisan would have been motivated to do so because Frutos et al. specifically recommend using covalent bonding of the polymer (e.g., MAST) to a biomolecule for immobilization. The ordinary artisan would have had a reasonable expectation that one could form an amide bond between the amino groups of a protein or peptide and maleic anhydride because Rodriguez et al. teach that maleic anhydride forms amide bonds.

The references are silent regarding the hydrophobic-absorptive and cell binding characteristics of laminin-1 to cells but meets the claimed limitations in that MAST is a linear polymer with a hydrophobic styrene group and that laminin-1 is bound to a MAST substrate which indicates that the claimed characteristics should be present in the prior

art invention as also as those instantly claimed. In this case, burden is shifted to the Applicant to distinguish the instant invention over the prior art.

It is noted that In re Best (195 USPQ 430) and In re Fitzgerald (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter which there is reason to believe naturally includes functions that are newly cited or is identical to a product instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter shown to be in the prior art does not possess characteristic relied on" (205 USPQ 594, second column, first full paragraph).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSAN HANLEY whose telephone number is (571)272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sue Liu can be reached on 571-272-5539. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Susan Hanley/
Primary Examiner, Art Unit 1653